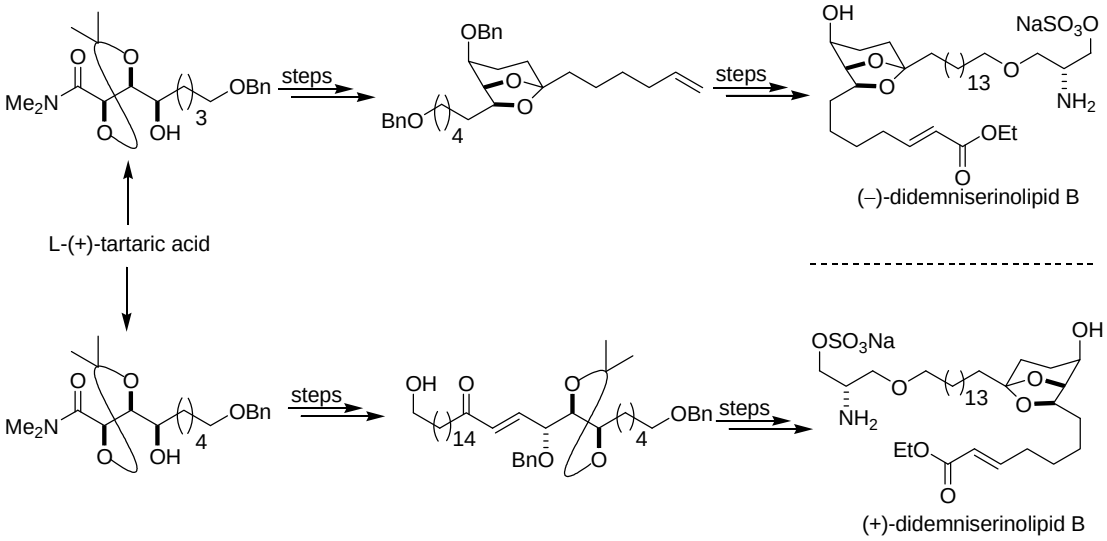
SYNOPSIS

The thesis entitled "***Enantioselective synthesis of didemniserinolipid, cladospolides, aspercyclide and muricatacin"*** is divided into three chapters.

First chapter of the thesis deals with the formal total synthesis both enantiomers didemniserinolipid B from L-(+)-tartaric acid. Fused bicyclic acetals containing 6,8-dioxabicyclo[3.2.1]octane structural unit are wide spread in bio active natural products. Didemniserinolipids A-C possessing similar framework were isolated from a methanol extract of *Didemnum* sp., and some of the analogous compounds were found to be cytotoxic against P388, A549, and HT29 tumor cell lines. Pivotal reactions *en route* to the natural product include the elaboration of a γ-hydroxy amide derived from tartaric acid, olefin cross metathesis and Wittig olefination (Scheme 1).

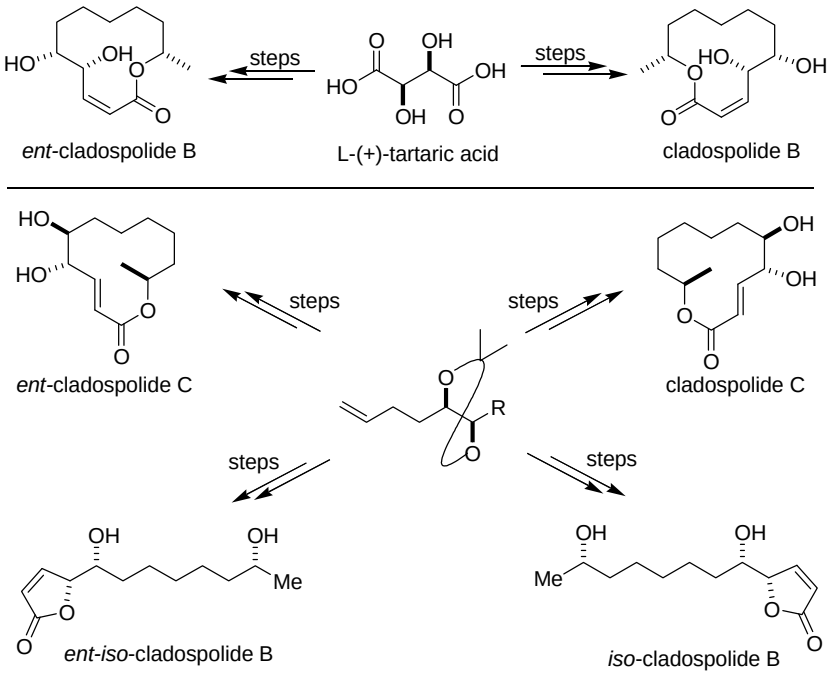


Scheme 1: Retrosynthesis of both enantiomers of didemniserinolipid B.

Second chapter of the thesis describes an enantiodivergent synthesis of macrolactones:

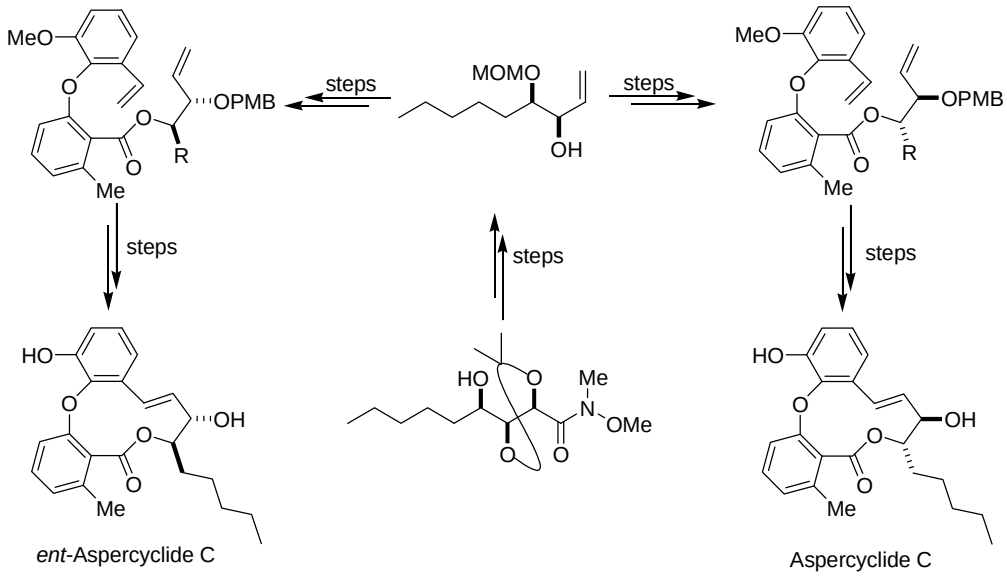
In **section A**, enantiodivergent approach for the synthesis of cladospolides B, C and *iso*-cladospolide B is described. The cladospolides A-D are a class of 12-membered macrolactones, isolated from various cladosporium species of fungi and posseses a range of

biological activities. Key reaction in the synthetic sequence involve formation of the required side chain by olefin cross metathesis. Selective Wittig olefination and lactonization afforded cladospolides (Scheme 2).



Scheme 2: Enantiodivergent synthesis of cladospolide B, C and *iso*-cladospolide B.

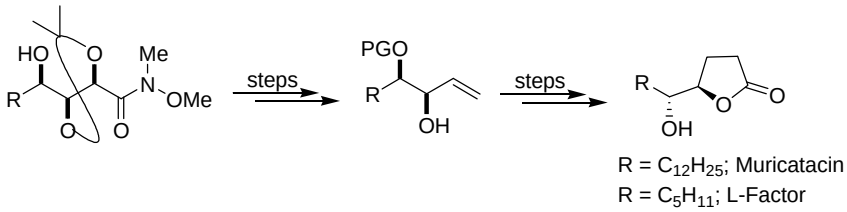
In **section B**, synthesis of bio-active biaryl ether lactone aspercyclide is described. Aspercyclides A-C are 11-membered biaryl ether lactones isolated from the extraction of the fermentation broth of an *Apergillus. Sp.*. Aspercyclides are reported to be moderately active (IC_{50} of 200 μM for aspercyclide A) in the IgE receptor binding, which is key for the understanding of allergic disorders. A combination of Boord elimination and Mitsunobu reactions were employed to synthesize the key homoallylic alcohol from γ-hydroxy amide derived from tartaric acid. Elaboration of γ-hydroxy amide derived from L-(+)-tartaric acid is the key step for the synthesis of both enantiomers of the chiral homoallylic alcohol part, while Ullmann coupling reaction is employed to construct biaryl linkage. Ring closing metathesis (RCM) of the diene furnished required macrolactone (Scheme 3).



Scheme 3: Enantiodivergent formal total synthesis of aspercyclide C.

Last chapter of the thesis describes the enantioselective synthesis of muricatacin, a bio-active butanolide isolated as the major component of a scalemic mixture from the seeds of *Annona muricata.* Muricatacin was found to exhibit potent cytotoxicity toward several human tumor cell lines with SAR studies showing that activity is influenced significantly by the nature of the side chain.

Stereoselective synthesis of (−)-Muricatacin and structurally similar butanolide L-Factor has been accomplished from L-(+)-tartaric acid. Pivotal strategy in the synthesis is the elaboration of *γ*-hydroxy amide to the required allylic alcohol which on further reactions (including RCM) provided muricatacin (Scheme 4).



Scheme 4: Stereoselective synthesis of Muricatacin and L-Factor.